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Base-free β-boration of α,β-unsaturated imines catalysed by Cu_2O with concurrent enhancement of asymmetric induction

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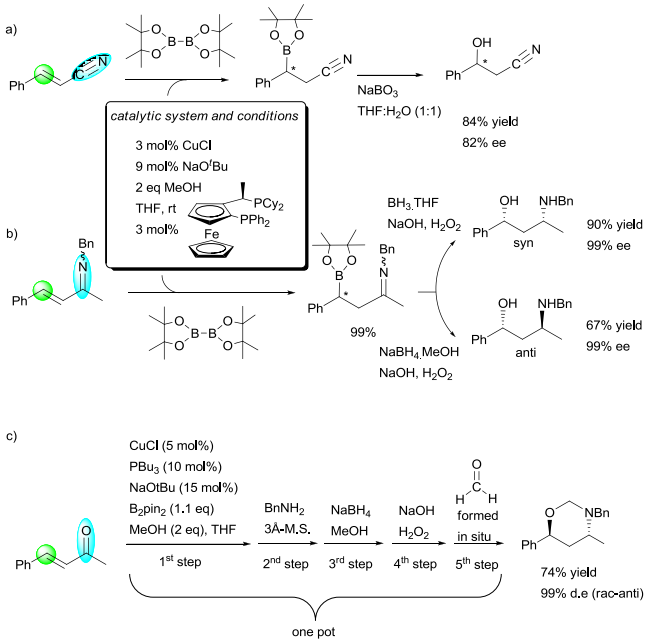
Dedication ((optional))

The stereoselective synthesis of y-aminoalcohols via the catalytic asymmetric β-boration of unsaturated imine precursors has been streamlined with the use of Cu_2O as catalyst, readily accessible (*R*)-Binap chiral ligands and no additional base. The new simplicity of the catalytic system has the added value of in situ formation of the imines, allowing access to chalcone-ketone derivatives, and aliphatic cyclic and acyclic ketones. The reaction was also followed using in situ IR spectroscopy, demonstrating the imine formation-borylation sequence and that the new catalytic system is superior to those employed for this reaction previously.

Introduction

Cu(I) catalysed asymmetric β-boration reactions have received considerable attention since Yun *et al*. discovered that CuCl (3 mol%) modified with bidentate Josiphos-type chiral ligands (3 mol%) could activate B_2pin_2 in the presence of base (9 mol%), to deliver the Bpin moiety enantioselectively to the β-position of α,β-unsaturated nitrile compounds (Scheme 1a).[1] Further efforts have been devoted to increase the scope of application of this convenient methodology to polyfunctional organoboron compounds.[2,3] We became interested in, and focussed on, the preparation of γ-aminoalcohols in a highly enantio- and diastereo-selective manner *via* a Cu(I) mediated β-boration of α,β-unsaturated imines followed by a boron-assisted *in situ* imine reduction and B-C oxidation steps (Scheme 1b).[4] We extended this strategy using *in situ* formation of the α,β-unsaturated imines from α,β-unsaturated aldehydes and ketones, trapping them using the β-borylation.[5] In addition for certain water-soluble γ-amino alcohol products especially, a further protection step could be performed *in situ* to give the readily isolated 1,3-oxazine derivatives in a 5 step-one pot sequence (Scheme 1c).[5]



Scheme 1. Strategies of precise C-B bond formation with CuCl: a) ref. 1, b) ref. 4a, c) ref. 5.

For all the Cu-mediated β-borations of electron deficient olefins reported to date, the addition of base has always been required,[6] unless preformed (NHC)CuOR species (NHC= N-heterocyclic carbene ligands) and $Cu(OH)_2$/L are used to activate the B_2pin_2[7,8] or sp^2-sp^3 hybridized mixed diboron reagents, generating the CuBpin reactive species the CuCl catalyst.[9] We became interested in exploring the use of Cu_2O as precursor of the active catalytic system for the β-boration of α,β-unsaturated imines. Most importantly, this could potentially behave as a novel

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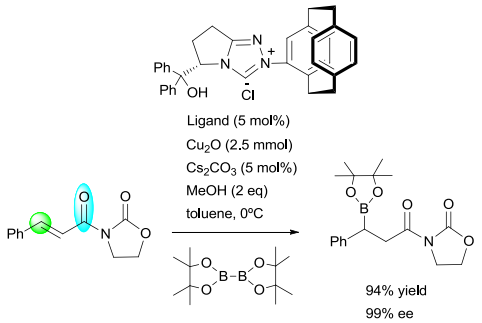
base-free system, as well as potentially being asymmetric when used in the presence of suitable compatible chiral ligands. This hypothesis is based on the possibility that Cu_2O could interact with MeOH to generate a Cu(I)-alkoxide or -hydroxide species. To the best of our knowledge, there is only one example of asymmetric induction upon C-B bond formation mediated by Cu_2O in the β-boration of α,β-unsaturated *N*-acyloxazolidinones using a chiral bicyclic 1,2,4-triazolium salt (Scheme 2) and Cs_2CO_3 base.[10] Our objective was to investigate, and highlight the benefits of, Cu_2O as a cheap catalyst precursor, avoiding the addition of an external base and with the potential of being modified with cheap, commercially available chiral ligands, such as BINAP.



Scheme 2. Cu_2O mediated β-boration of *N*-cinnamoyloxazolidin-2-one with chiral triazoliuim salt.

Results and Discussion

Our study began with the β-boration of 4-phenyl-3-buten-2-one **1** as a model substrate, and B_2pin_2 as the diboron reagent. Two Cu(I) sources were selected, CuCl (3 mol%) and Cu_2O (1.5 mol%), in order to compare their relative activities as catalyst precursors, in the presence of (*R*)-BINAP. In an initial experiments in the absence of $BnNH_2$, the substrate **1** was not converted into the β-borated ketone **2**, (Table 1, entries 1 and 6), however, with the increasing addition of $BnNH_2$ (10 – 100 mol%) progressive formation of the β-borated imine **3a** ocurred with different efficiency, depending on the copper source. When the CuCl-(*R*)-BINAP catalytic system was used, the β-borated ketone **2** was still the main product at low amine loadings (Table 1, entries 2-3). When the percentage of amine increased from 50 to 100%, only β-borated imine **3a** was observed, although substrate **1** still remained even in the presence of 100% of $BnNH_2$ (Table 1, entries 4-5). Remarkably however, when Cu_2O-(*R*)-BINAP catalyst system was used for the β-boration of **1**, the percentage of the β-borated imine **3a** formed was, in all the cases, close to the percentage of amine present (Table 1, entries 7-10). This shows that Cu_2O favours trapping of the "*in situ*" formed α,β-unsaturated imine by catalysing its transformation into the corresponding β–borated imine **3a** and is unreactive to the starting unsaturated ketone. In addition, the beneficial influence of Cu_2O could also be extended to the asymmetric induction of the C-B bond formation step. While the CuCl-(*R*)-BINAP catalytic system provided the β-borated imine with e.e. values around 85-89%, the Cu_2O-(*R*)-BINAP system promoted the enantioselective formation on **3a** in up to 99 % of e.e. (Table 1). It is noteworthy also that the remaining β-borated ketone **2** was obtained always with e.e. values between 16-22%, and that an excess of (*R*)-BINAP in the reaction media did not change the reaction outcome (Table 1, entry 11). The same was also found to be the case with higher loadings of Cu_2O, (Table 1, entry 12). Interestingly, when a Cu(II) source was used instead, i.e. CuO, the catalytic system CuO-(*R*)-BINAP did convert the α,β-unsaturated ketone **1** into the β-borated imine **3a**, however, with ony 71% yield and only moderate e.e.s (Table 1, entry 13). Apart from the two previous reports of Cu(II) catalysed β-boration of α,β-unsaturated carbonyl compounds,[8,11] to the best of our knowledge, this is the first example of Cu(II) catalysing the β-boration of α,β-unsaturated imines. It is also interesting to observe that the nature of the amine used in the reaction seems to be crucial for the enantioselection. Hence, when the β-boration of **1** with Cu_2O-(*R*)-BINAP was carried out in the presence of 100 mol% of NH_2Bu, the β-borated imine **3b** was exclusively formed in high yield, but only with 27% of e.e. (Table 1, entry 14).

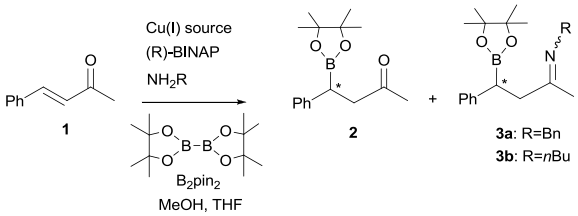
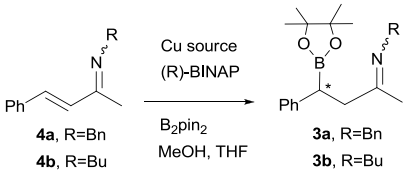


Table 1. Cu-(*R*)-BINAP mediates β-boration of activated olefins.[a]

Entry	Cu(I)	RNH_2 (mol%)	Conv (%)[b]	**2** (%)[b]	e.e (%)[c]	**3**(%)[b] [IY(%)]	e.e (%)[c]
1	CuCl	---	0	---	---	---	---
2	CuCl	$BnNH_2$ (10)	24	21	21 (*S*)	3	nd
3	CuCl	$BnNH_2$ (25)	35	32	22 (*S*)	3	nd
4	CuCl	$BnNH_2$ (50)	36	---	---	36	89 (*S*)
5	CuCl	$BnNH_2$ (100)	71	---	---	71	85 (*S*)
6	Cu_2O	---	0	---	---	---	---
7	Cu_2O	$BnNH_2$ (10)	43	37	16 (*S*)	6	99 (*S*)
8	Cu_2O	$BnNH_2$ (25)	53	32	22 (*S*)	21	99 (*S*)
9	Cu_2O	$BnNH_2$ (50)	57	11	nd	46	95 (*S*)
10	Cu_2O	$BnNH_2$ (100)	>99	0	nd	99	95 (*S*)
11[d]	Cu_2O	$BnNH_2$ (100)	>99	0	nd	99	93 (*S*)
12[e]	Cu_2O	$BnNH_2$ (100)	>99	0	nd	>99 [89]	95 (*S*)
13[f]	CuO	$BnNH_2$ (100)	71	0	nd	71	73 (*S*)
14	Cu_2O	n-$BuNH_2$ (100)	>99	---	---	99	27[g] (*S*)

[a] Reaction conditions: substrate (0.25 mmol), CuCl (3 mol%) or Cu_2O (1.5 mol%), (*R*)-BINAP (3 mol%), B_2pin_2 (1.1 equiv.), MeOH (2.5 equiv.), THF (1 mL) 25 ºC, 16 h. [b] Conversion and selectivity calculated from consumed substrate by ^1H NMR. [c] E.e. calculated by HPLC-UV as an average of two results. [d] Cu_2O (1.5 mol%), (*R*)-BINAP (6 mol%). [e] Cu_2O (3 mol%), (*R*)-BINAP (6 mol%). [f] CuO (3 mol%), (*R*)-BINAP (6 mol%). [g] E.e. calculated on the hydrolysed ketone *via* HPLC-MS.

To confirm the benefits of Cu_2O-(*R*)-BINAP on the enantioselective formation of the β-borated imines **3**, we became interested in isolating the α,β-unsaturated imines, such as (*E*)-1-phenyl-N-(4-phenylbut-3-en-2-ylidene)methanamine **4a**, and performing the β-boration on that substrate to compare with the reactions carried out from the *in situ* reaction of α,β-unsaturated ketone **1** + $BnNH_2$. In the absence of base, Cu_2O-(*R*)-BINAP catalysed the formation of **3a** with high enantioselectivity, while CuCl-(*R*)-BINAP was inactive (Table 2, entries 1 and 2). The addition of 10 mol% NaOtBu or Cs_2CO_3 to the CuCl-(*R*)-BINAP catalyst system favoured the formation of **3a**, but resulting in a racemic product (Table 2, entries 4 and 5). However, the addition of 10 mol% $BnNH_2$ as base did not favour the β-boration of the imine. The role of the base is expected to favour transmetallation between CuCl and B_2pin_2,[6] however, it seems that only inorganic bases assist this step. In contrast, when Cu_2O was used, no additional base was required to promote the transmetallation and in addition, the enantioselectivity was significantly higher.



4a, R=Bn
4b, R=Bu

3a, R=Bn
3b, R=Bu

Table 2. Cu-(*R*)-BINAP mediates β-boration of activated olefins[a]

Entry	Imine	Cu(I)	Base (mol%)	Conv (%)[b]	**3** (%)[b] [IY(%)]	e.e (%)[c]
1	**4a**	Cu_2O	---	>99	>99	87 (S)
2	"	CuCl	---	0	---	--
3	"	CuCl	$BnNH_2$ (10)	0	---	--
4	"	CuCl	$CsCO_3$ (10)	>99	>99	0
5	"	CuCl	NaOtBu (10)	>99	>99	0
6	"	$(CH_3CN)_4$ $CuPF_6$	---	>99	>99	85 (S)
7	"	CuO	---	15	15	69 (S)
8	**4b**	Cu_2O	---	99	99	7[d] (S)
9	"	$(CH_3CN)_4$ $CuPF_6$	---	99	99	8[d] (S)
10	"	CuCl	---	<5	---	--

[a] Reaction conditions: α,β-unsaturated imine (0.25 mmol), CuCl (3 mol%)/(*R*)-BINAP (6 mol%), $(CH_3CN)_4CuPF_6$ (3 mol%)/(*R*)-BINAP (6 mol%) or Cu_2O (1.5 mol%)/(*R*)-BINAP (3 mol%), B_2pin_2 (1.1 equiv.), MeOH (2.5 equiv.), THF (1 mL) 25 ºC, 16 h. [b] Conversion calculated from consumed substrate by ^1H NMR. [c] E.e. calculated by HPLC-UV as an average of two results. [d] E.e. calculated from the hydrolysed ketone via HPLC-MS.

The lack of a coordinating anion on the Cu(I) catalytic system appears to be the key factor in avoiding the need for additional base in the β-boration. This is clearly demonstrated by using $Cu(CH_3CN)_4PF_6$ modified with (*R*)-BINAP to catalyse the asymmetric β-boration of **4a** (Table 2, entry 6), which is similar to using Cu_2O, however, Cu_2O significantly cheaper. Interestingly, when Cu(II) was also explored for catalysing the reaction, we observed that the CuO-(*R*)-BINAP catalytic system was almost inactive towards the β-boration of **4a** (Table 2, entry 7). If we compare the latter result with the CuO-(*R*)-BINAP catalysed β-boration of **1** in the presence of 1 eq of $BnNH_2$ (Table 1, entry 13), we can conclude that the Cu(II) catalytic system studied needs a base to activate the diboron source. From these observations, it is clear that the use of Cu_2O is especially beneficial because it can be used in the absence of bases to promote the desired β-boration reaction. In contrast, when the Cu_2O-(*R*)-BINAP mediated β-boration of (*E*)-N-(4-phenylbut-3-en-2-ylidene)butan-1-amine **4b**, also without base was carried out, the β-borated imine **3b** was formed quantitatively, however, with low enantioselectivity (Table 2, entry 8). Similar behaviour was observed when $Cu(CH_3CN)_4PF_6$ was the copper source, however, CuCl resulted in inactivity (Table 2, entries 9 and10). The observation of low enantioselectivity in entries 8 and 9 (Table 2) also confirms the important of the N-substituent in achieving high asymmetric induction.

The synergy between Cu_2O and (*R*)-BINAP (**L0**) wasfurther demonstrated when we explored the influence of alternative bidentate chiral ligands such as (*R*)-Tol-BINAP (**L1**), (*R*)-Ph-MeOBiphep (**L2**), Josiphos (**L3**, **L4**) and Mandiphos (**L5**) type ligands. Remarkably, the cheapest ligand, (*R*)-BINAP, provided the best influence on the enantioselective Cu_2O-catalysed β-boration of 4-phenyl-3-buten-2-one **1**, in the presence of 1 eq. of $BnNH_2$ and B_2pin_2 (Figure 1).

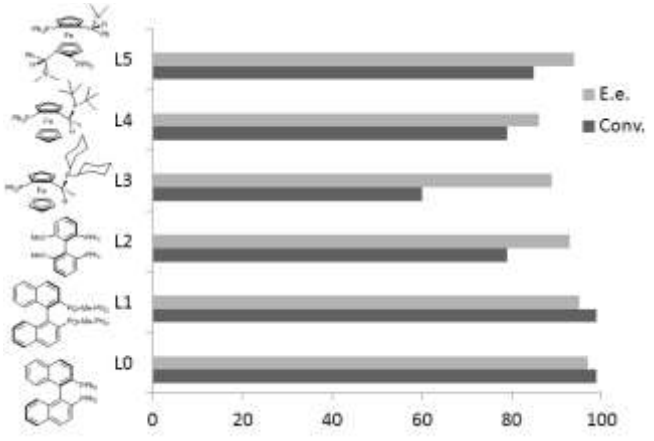


Figure 1. Cu_2O (1.5 mol%)/L (3 mol%), catalysed the β-boration of 4-phenyl-3-buten-2-one (**1**) (0.25 mmol), in the presence of $BnNH_2$ (1eq.) and B_2pin_2 (1.1 eq.), MeOH (2.5 equiv.), THF (1 mL) 25 ºC, 16 h.

The substrate scope of the β-boration of α,β-unsaturated imines, formed *in situ* from the corresponding α,β-unsaturated ketones and $BnNH_2$, was surveyed using Cu_2O-(*R*)-BINAP catalyst system, and compared also with the influence of alternative chiral ligands. For the transformation of 4-(*p*-MeO-phenyl)-3-buten-2-one **5** into the β-borated imine **6** (Table 3, entry 1), the Cu_2O-(*R*)-BINAP and Cu_2O-(*R*)-Tol-BINAP catalytic systems provided moderate conversions but high e.e.s. On the contrary, the Cu_2O system modified with the MeOBiphep (**L2**) and Mandiphos (**L5**) ligands favoured reaction conversion, but provided only moderate enantioselectivity. When the substrate studied was the more electron deficient olefin 4-(*p*-Cl-phenyl)-3-buten-2-one **7** (Table 3, entry 2), all the catalytic systems explored provided a quantitative β-borated product **8** with only moderate enantioselectivity.

Having examined acyclic substrates, β-boration of cyclic unsaturated imine substrates was studied. Towards this end, we found that cyclohexenone **9** could be efficiently converted into the desired product **10** with Cu_2O-modified by (*R*)-BINAP (**L0**), (*R*)-Tol-BINAP **L1** and MeOBiphep **L2**, however, the enantioselectivity was only moderate (Table 3, entry 3). In contrast, when the influence of a Walphos-type ligand **L6** was explored, we observed that although conversion to the product **10**

was low (20%), the e.e. was the highest (92%) (Table 3, entry 3). It is important to note that although this is the first approach to the enantioselective formation of cyclic β-boryl imine derivatives, the *base-free* asymmetric induction provided by Cu_2O modified with ligands **L0**, **L1** and **L6** is in complete agreement with the previous work of Yun and co-workers,[2f] who reported that CuCl+*base* mediated the enantioselective β-boration of cyclohexenone (Table 3, entry 4). Since the corresponding α,β-unsaturated cyclic imine, 1-phenyl-N-(cyclohexenyl)methanamine, could not be isolated to be β-borated, the alternative *in situ* formation of the imine, followed by β-boration trapping by means of the Cu_2O-based system, represents a simple method by which to obtain an enantiomerically enriched approach β-borated imine **10**.

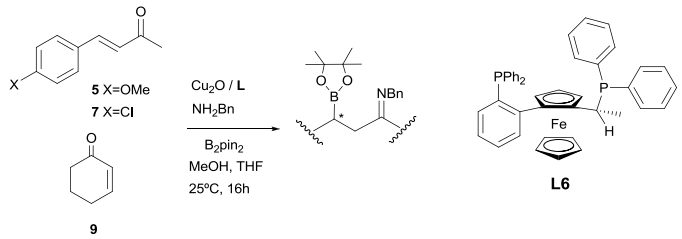
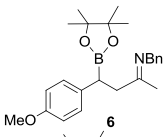
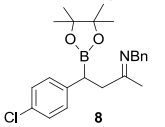
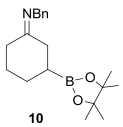
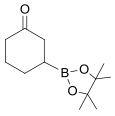


Table 3. Substrate scope for the Cu_2O mediated asymmetric β-boration of *in situ*-formed α,β-unsaturated imines. [a]

Entry	Product	Ligand	Conv (%)[b] [IY(%)]	e.e (%)[c]
1		(*R*)-BINAP **(L0)**	67 [45]	86 (*S*)
		L1	71	82 (*S*)
		L2	85 [60]	49 (*R*)
		L5	99	35 (*R*)
2		(*R*)-BINAP **(L0)**	99 [87]	48 (*S*)
		L1	99	47 (*S*)
		L2	99 [85]	58 (*S*)
		L5	99	35 (*S*)
3		(*R*)-BINAP **(L0)**	99 [89]	39 (*S*)[d]
		L1	99	65 (*S*)[d]
		L2	97	30 (*S*)[d]
		L6	20	92 (*R*)[d]
4		(*R*)-BINAP **(L0)**	93 (2 h)	40 (R)[e]
		L1	93 (2 h)	63 (S)[e]
		L6	90 (24 h)	90 (S)[e]

[a] Reaction conditions: α,β-unsaturated imine (0.25 mmol), Cu_2O (3 mol%), L (6 mol%), B_2pin_2 (1.1 equiv.), MeOH (2.5 equiv.), THF (1.3 mL) 25 ºC, 16 h. [b] Conversion calculated from consumed substrate by ^{1}H NMR spectroscopy. [c] E.e. calculated by HPLC-UV as an average of two results. [d] e.e. Calculated on the hydrolysed β-borated ketone *via* HPLC-MS. [e] Ref. 2f, CuCl (3 mol%), NaOtBu (3 mol%), L (3 mol%).

Another set of substrates we were keen to explore as suitable candidates for the *in situ* imine formation followed by β-boration, in the presence of Cu_2O/L, were the aliphatic, open-chain, α,β-unsaturated ketones, 4-hexen-3-one **11**, 3-hepten-2-one **13** and 3-nonen-2-one **15**. The corresponding α,β-unsaturated imines could also not be isolated in order to perform a copper-catalysed β-boration, and hence, the *in situ* protocol gave us an alternative approach towards the aliphatic β-borated imines (see Table 4). In all the cases, a secondary product (β-amino ketone) could be identified due to the competitive aza-Michael addition reaction of the amine to the α,β-unsaturated ketones. Therefore, the selectivity of the desired β-borated α,β-unsaturated imine varied from moderate to high, depending on the substrate and the nature of the chiral ligand. When the substrate was 3-hepten-2-one **13**, the two-step reaction occurred efficiently to give a high conversion to the β-borated imine (up to 93%, Table 4, entry 2). The bidentate chiral ligand that induced the highest enantioselectivity in the Cu_2O mediated β-boration of the corresponding imines of ketones **13** and **15** was the Josiphos-type ligand **L7** (e.e.s 70-92%, Table 4, entries 2 and 3).

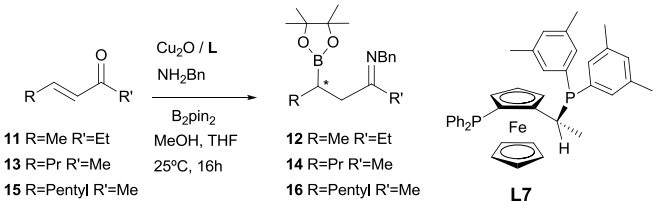
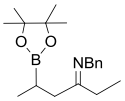
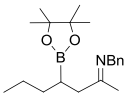
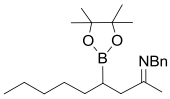


Table 4. Substrate scope for the Cu_2O mediated asymmetric β-boration of in situ-*formed* α,β-unsaturated imines from aliphatic open chain α,β-unsaturated ketones. [a]

Entry	Product	Ligand	Conv (%)[b]	Sel(%)[c] [IY(%)]	e.e (%)[d]
1		(*R*)-BINAP	99	55 [35]	66 (+)
		L1	99	63	61(+)
		L2	99	68 [32]	50 (+)
		L7	99	54	80 (+)
2		(*R*)-BINAP	99	70 [63]	62 (+)
		L1	99	93	60 (+)
		L2	99	90 [76]	64 (+)
		L7	99	52	73 (+)
3		(*R*)-BINAP	99	71 [56]	70 (+)
		L1	99	77	66 (+)
		L2	99	58 [43]	64 (+)
		L7	99	64	92 (+)

[a] Reaction conditions: α,β-unsaturated imine (0.25 mmol), Cu_2O (3 mol%), (*R*)-BINAP (6 mol%), B_2pin_2 (1.1 equiv.), MeOH (2.5 equiv.), THF (1.3 mL) 25 ºC, 16 h. [b] Conversion calculated from consumed substrate by ^{1}H NMR spectroscopy. [c] Selectivity calculated by ^{1}H NMR spectroscopy, with the β-amino ketone as by-product. [d] e.e. Calculated via HPLC-MS.

We further examined this *base-free* system by following the reaction between **1** and $BnNH_2$ (*in situ* imine formation) with subsequent trapping *via* our Cu_2O-**L1**-B_2pin_2-derived boron nucleophile to give the β-boryl imine **3a** (Figure 2). Additionally, we followed the same reaction using CuCl as our Cu (I) salt (Figure 3). For completion we also monitored the catalytic borylation of cyclehexenone derived imine using the Cu_2O-**L1**-B_2pin_2 system. This was made possible by *in situ* IR spectroscopy (ReactIR). In each case, the initial 20 min have been cropped to allow for addition/mixing of reagents, imine formation, and the addition of MeOH which initiates the β-boration (measured by the loss of the B_2pin_2, blue line, Fig. 2, 3 and 4). In each case, the formation of the imine product is shown in green. The loss of the initial carbonyl has been omitted for clarity (see ESI for complete profiles).

The reaction of the chalcone **1**-derived imine **4a** follows a first-order-like reaction profile (Fig. 2a), reaching completion after ca. 10 h (Note: subsequent addition of borohydride-MeOH can be followed readily also by ReactIR, with the imine reduction clearly visible, see SI). Interestingly, the formation of **3a** almost mirrors the rate-of-loss of B_2pin_2, (see Fig. 2b: graphical output of Fig. 2a) and is exceeded by the loss of enone **1**, thus providing further

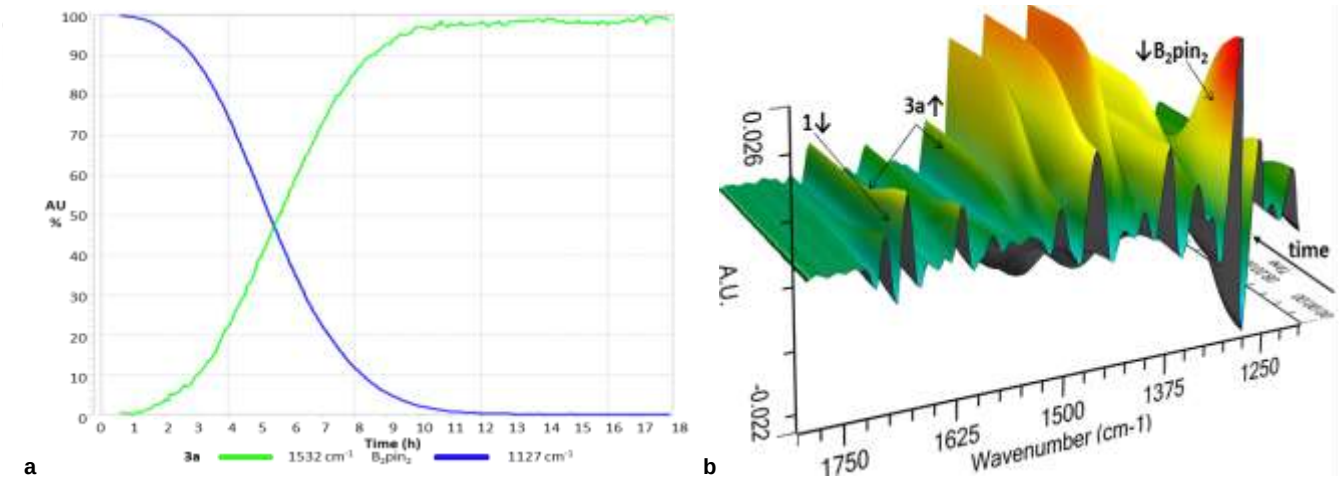
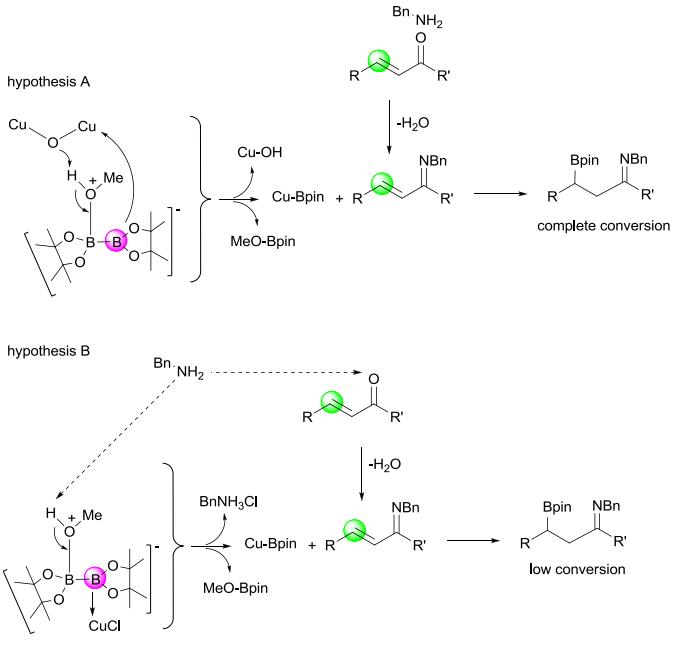


Figure 2. a) ReactIR derived reaction profile showing synchronous *in situ* imine **4a** formation from ketone **1** and Cu_2O-**L1** catalysed borylation, forming β-boryl imine **3a.** Due to overlapping C=O (substrate) and C=N (product) stretches, an alternative stretch at 1532 cm^{-1} was followed to monitor the formation of **3a**; ***b)*** The corresponding ReactIR graphical output (with 2nd derivative base-line correction) showing synchronous *in situ* imine **4a** formation from ketone **1** and Cu_2O-**L1** catalysed borylation, forming β-boryl imine **3a**.

further evidence that the reaction proceeds throughout imine formation-borylation, and not the borylation of **1** followed by subsequent imine formation. Indeed, this highlights the distinct role, when compared to the analogous carbonyl species, that α,β-unsaturated imines have in the Cu-catalysed β-boration reaction; they are considerably more reactive towards the borylation reaction than the unsaturated ketone. In stark contrast, when the identoical reaction is cariied out using CuCl (see ESI for full profile) in place of Cu_2O, the reaction shows completely different kinetic behaviour and does not proceed to completion even after 24 h. Interestingly Fig. 3 shows the important role of the base in the case of CuCl. Indeedm addition of NaO*t*Bu (10 mol%) after 4 hours results in the complete loss of the B_2pin_2 and full conversion to the imine **3a**. Moreover, Fig. 4 demonstrates the similarity of behaviour of the *in situ* cyclohexenone-derived imine borylation to that of the chalcone system, *i.e.* the loss of substrate **10** and B_2pin_2 is synchronous to the gain β-boryl imine **9**. However, the reaction is slightly faster, being complete in essentially 6 (for **9**) *vs.* 10 h (for **3a**). This strongly suggests that



Scheme 3. Hypothetical activation of B_2pin_2 with Cu_2O and CuCl.

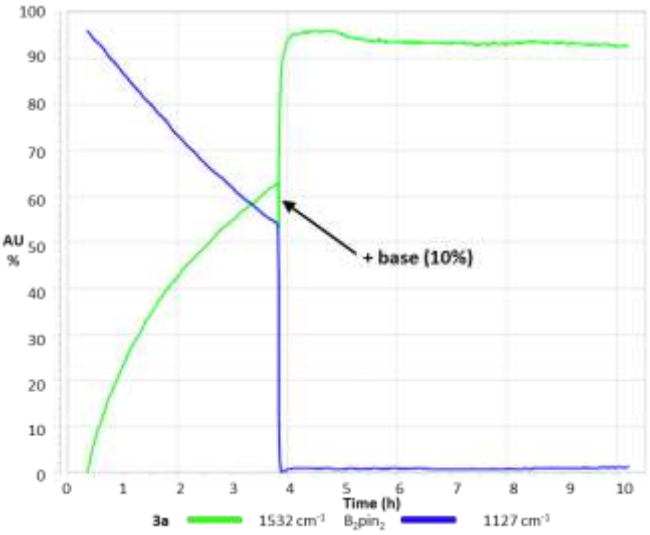


Figure 3. ReactIR derived reaction profile showing synchronous *in situ* imine **4a** formation and borylation to give the resulting imine **3a** (CuCl-**L1**+ the addition of NaO*t*Bu (10 mol%) after 4 hours). The peak-fluctuation at 4 hours is a result of mixing on addition of base.

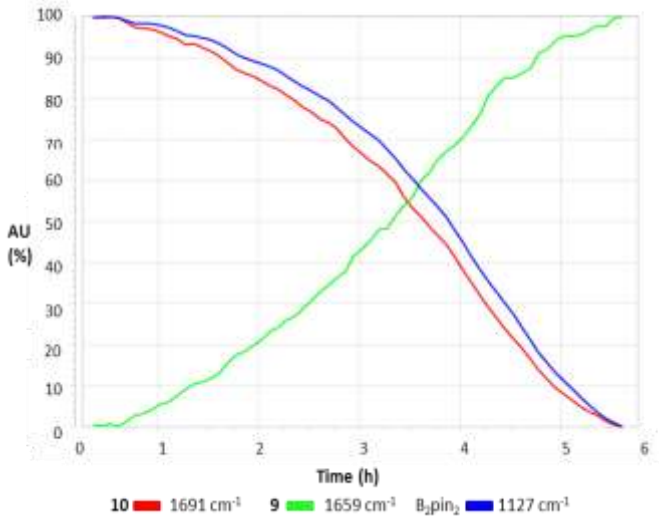


Figure 4. ReactIR derived reaction profile showing synchronous *in situ* imine derivative of ketone **9** and Cu_2O-**L1** catalysed borylation, forming β-boryl imine **10**.

N-Cu chelation is neither necessary for the unsaturated imine borylation reaction, nor is an s-cis conformation of the unsaturated imine more reactive towards borylation. Indeed, the fixed s-trans conformation derived from the cyclohexenone imine is more reactive, clearly illustrating this point.

Scheme 3 illustrates, in hypothesis A, a plausible interaction between Cu_2O, MeOH and B_2pin_2, to provide the corresponding CuBpin nucleophilic species and an additional Cu(OH) species ready to transmetallate further B_2pin_2. In this picture hypothesis, the NH_2Bn seems to be exclusively involved in imine formation. However, when CuCl is used as the copper source, the $BnNH_2$ may have a partial role of activating MeOH and forming the imine (Scheme 3, hypothesis B). This explains why the reactions carried without base addition and using CuCl do not proceed to completion and low or inactivity is observed in the β-boration of the isolated imine.

Conclusion

In conclusion, we have found that Cu_2O guarantees the clean and efficient β-boration of unsaturated imines in the absence of bases. Both the *in situ* formation of the α,β-unsaturated imine and concurrent β-boration of this intermediate can be readily followed by *in situ* IR spectroscopy, which shows a clean and rapid pseudo first order reaction, which is slightly faster for the a cyclic enone-derived imine compared with the acyclic system. The activation of the diboron reagent, B_2pin_2, with Cu_2O does not need external base to form the CuBpin moiety. The modification of Cu_2O with commercially available chiral ligands, such as (*R*)-BINAP, enhances the asymmetric induction on the C-B bond formation, principally when the Bn group is attached to the imine.

Experimental Section

Experimental procedure for the copper/(*R*)-BINAP catalyzed β–boration of *in situ* formed α,β–unsaturated imines with bis(pinacolato)diboron.

Cu(I) salts (1.5-3 mol%), (*R*)-BINAP (3-6 mol%, 0.0075-0.015 mmol, 4.7-9.3 mg) were transferred to a Schlenck tube and dissolved in THF (1 mL) under Ar. After 15 min, bis(pinacolato)diboron (70 mg, 0.28 mmol, 1.1 equiv.) was added to the solution and stirred during 10 min. Then benzylamine (0.25 mmol, 27 µl) and benzylideneacetone (0.25 mmol, 36.5 mg) were added at the same time. Finally, MeOH (0.55 mmol, 25 µl, 2.5 equiv.) was added and the reaction mixture was left to stir overnight at RT. The reaction products and conversions were determined by ^{1}H NMR. The e.e.s were determined directly by HPLC-UV or HPLC-MS for the hydrolysed β–borated ketone.

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Keywords: α,β-unsaturated imines • β-boration • Cu_2O • enantioselectivity • β-boryl imines

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